

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date  
20 January 2005 (20.01.2005)

PCT

(10) International Publication Number  
**WO 2005/005616 A3**

(51) International Patent Classification<sup>7</sup>: C12N 1/00, 5/00, C12P 13/04, C07B 59/00, G01N 33/58, 33/68

GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number:  
PCT/NL2004/000503

(22) International Filing Date: 12 July 2004 (12.07.2004)

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
PCT/NL03/00514 11 July 2003 (11.07.2003) NL

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
2 June 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(71) Applicant and

(72) Inventor: EGOROVA-ZACHERNYUK, Tatiana, A. [NL/NL]; Spieghelstraat 16a, NL-2332 BD Leiden (NL).

(74) Agent: VAN WESTENBRUGGE, Andries; Nederlandse Octrooibureau, Scheveningseweg 82, P.O. Box 29720, NL-2502 LS The Hague (NL).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,

WO 2005/005616 A3

(54) Title: COMPOSITIONS AND METHODS FOR STABLE ISOTOPE LABELLING OF BIOLOGICAL COMPOUNDS

(57) Abstract: The present invention is concerned the labelling of biological compounds with stable isotopes such that the three-dimensional structure of the biological compounds may be analysed by e.g. NMR spectroscopy. The invention employs microorganisms that are grown on mineral media comprising carbon and nitrogen sources that contain stable isotopes to produce biomass that is uniformly labelled with stable isotopes. The biomass may be autolysed to produce an autolysate. The biomass may further be extracted with organic solvent to produce lipids. The (delipidised) biomass is hydrolysed to produce labelled amino acids and other nutrients, which are used together with the autolysate, extracted lipids and further components to compose a culture medium for a mammalian or insect host cells for the production of biological compounds that are uniformly labelled with stable isotopes. The biological compound preferably is a biological acromolecule, such as e.g. a mammalian membrane protein.